



NOTES

IMPRINTING DISORDERS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Genetic, epigenetic mutations/defects within imprinting controlling regions of genes
- Disruption of methylation of cytosine bases in CpG dinucleotides of DNA

RISK FACTORS

- Increased incidence in individuals conceived using assisted reproductive technology

SIGNS & SYMPTOMS

- Angelman syndrome
 - Seizures, severe intellectual disability, jerky/tremulous limbs, characteristic facial appearance (e.g. large mouth, protruding tongue, prominent nose), excitability, impaired speech
- Beckwith–Wiedemann syndrome
 - Premature birth, abdominal wall defects, embryonal tumors
- Prader–Willi syndrome
 - **Infancy:** poor feeding, low muscle tone, weak cry, diminished reflexes
 - Early childhood obesity, developmental delay, behavioral problems
 - Dysmorphic facial features

DIAGNOSIS

OTHER DIAGNOSTICS

- History, clinical examination
- Fluorescence in situ hybridization (FISH), genotyping, methylation DNA testing
- Methylation-sensitive multiplex ligation probe analysis (MS-MLPA)

TREATMENT

MEDICATIONS

- *Angelman syndrome:* antiepileptic therapy
- *Prader–Willi syndrome:* thyroid, sex hormone replacement therapy

OTHER INTERVENTIONS

- *Angelman syndrome:* speech therapy
- *Beckwith–Wiedemann syndrome:* tumor surveillance, abdominal wall repair
- *Prader–Willi syndrome:* food restriction, vitamin D/calcium supplements

VISIT...

LANZAROTE
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ANGELMAN SYNDROME

osms.it/angelman-syndrome

PATHOLOGY & CAUSES

- Genetic neurological disorder; severe developmental delay, intellectual disability, absence of speech, ataxia, dysmorphic features, unprovoked episodes of laughter

CAUSES

- Maternal 15q11-q13 deletion
- Loss of function of *UBE3A*
- Paternal uniparental disomy 15 (both copies of chromosome 15 from father)

SIGNS & SYMPTOMS

- Seizures, severe intellectual disability
- Ataxia, toe-walking, jerky/tremulous limbs
- Hypopigmentation, microcephaly, maxillary hypoplasia, large mouth, protruding tongue, prominent nose, wide-spaced teeth
- Inappropriate laughter ("happy puppet"), excitability, impaired speech

DIAGNOSIS

OTHER DIAGNOSTICS

- FISH, genotyping, methylation DNA testing

TREATMENT

MEDICATIONS

- Antiepileptic therapy for seizures

OTHER INTERVENTIONS

- Speech therapy; emphasis on nonverbal methods of communication

BECKWITH–WIEDEMANN SYNDROME

osms.it/beckwith-wiedemann_syndrome

PATHOLOGY & CAUSES

- Pediatric overgrowth syndrome; visceromegaly, predisposition to tumors

CAUSES

- Error in imprinted gene expression in chromosome 11p15.5 region
- Usually sporadic, may be inherited in autosomal dominant fashion

SIGNS & SYMPTOMS

- Fetal macrosomia, premature birth
- [Macroglossia](#)
- Renal medullary hyperplasia
- [Abdominal wall defects](#)
 - Omphalocele, umbilical hernia, diastasis recti
- Hypoglycemia due to islet cell hyperplasia
- Puberty, episeal fusion (early symptoms)
- Embryonal tumors (e.g. [Wilms tumor](#), hepatoblastoma, neuroblastoma, rhabdomyosarcoma)

DIAGNOSIS

OTHER DIAGNOSTICS

- Clinical diagnosis
- MS-MLPA
 - Detect majority of epigenetic, genetic etiologies

TREATMENT

OTHER INTERVENTIONS

- Tumor surveillance with abdominal MRI/CT scan
- Abdominal wall repair for omphalocele
- Assess, treat airway insufficiency; feeding evaluation in presence of macroglossia
- Assess, treat hypoglycemia for neonates

PRADER-WILLI SYNDROME

osms.it/prader-willi_syndrome

PATHOLOGY & CAUSES

- Genetic multisystem disorder; weak muscle tone; delayed growth, development; behavioral abnormalities (e.g. insatiable hunger)

CAUSES

- Paternal 15q11-q13 deletion (maternal gene unchanged)
- Maternal uniparental disomy 15 (both copies of chromosome 15 from mother)
- Defects in imprinting center controlling chromosome 15 activity of genes
- Associated with dysregulation of hypothalamic-pituitary axis

COMPLICATIONS

- Sleep apnea (central/obstructive), scoliosis, osteoporosis, hypothyroidism, Type II diabetes

SIGNS & SYMPTOMS

- Infancy
 - Poor feeding, low muscle tone, weak cry, diminished reflexes
- Overeating (hyperphagia), early childhood obesity
- Developmental delay
 - Intellectual disability; delayed motor, language development
- Behavioral problems
 - Inflexibility, obsessive-compulsive characteristics
- Low sex hormones in childhood, hypogonadism/hypogonadism; cryptorchidism in individuals who are biologically male

- Dysmorphic facial features in childhood
 - Almond-shaped eyes, narrow forehead, thin upper lip
- Small hands/feet, short stature

DIAGNOSIS

OTHER DIAGNOSTICS

- History, clinical examination
- Fluorescence in situ hybridization (FISH), genotyping, methylation DNA testing

TREATMENT

MEDICATIONS

- Human recombinant growth hormone therapy
 - Decrease body weight/fat, increase muscle mass
- Address complications
 - Thyroid, sex hormone replacement therapy

OTHER INTERVENTIONS

- Food restriction
- Address complications
 - Vitamin D, calcium supplements